UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

Date: March 07, 2012

Subject: **Iprodione:** Occupational Exposure and Risk Assessment for the Proposed New Uses on Cucurbits, Fruiting Vegetables (includes Updated Non-Occupational Cancer Assessment).

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Introduction

This memorandum addresses the occupational exposure and risk from the registrant's requested new uses for iprodione on curcurbits and fruiting vegetables. Additionally, this memo updates the non-occupational (i.e., residential) cancer assessment. This memorandum was reviewed by the Exposure Science Advisory Committee (ExpoSAC) on June 16, 2011. This assessment contains potentially compensable turf transferable residue data generated by Rhône-Poulenc (44968001) for iprodione.

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Executive Summary
The Health Effects Division (HED) has conducted an occupational exposure assessment for the proposed new uses of the fungicide and nematicide active ingredient (ai) iprodione on cucurbits and fruiting vegetables. The new agricultural uses are for the product Enclosure™ 4 Flowable, a liquid concentrate formulation (41.6% iprodione; 4 lbs iprodione per gallon) and are intended as a nematicide. Iprodione applications can be made mechanically (groundboom) or by chemigation. This memorandum addresses the occupational exposure and risk from this label amendment and the revised residential exposure assessment that is needed for a aggregate risk assessment.

The new use label-required personal protective equipment (PPE) for mixers/loaders is long-sleeved shirt, long pants, chemical-resistant footwear plus socks, chemical-resistant apron and chemical-resistant gloves.

Hazard Summary
Non-cancer short- and intermediate-term dermal and inhalation risk estimates in this assessment are based on systemic effects observed in the rat pubertal assay at the Lowest Observed Adverse Effect Level (LOAEL) of 50 mg/kg/day.

The non-cancer level of concern is an MOE of <1000 for the short- and intermediate-term exposure durations, respectively. The level of concern is based on uncertainty factors of 10x to account for intraspecies variability, a 10x for interspecies variability, and a factor of 10x to account for the LOAEL to NOAEL extrapolation for both short- and intermediate-term exposures.

Iprodione is also classified as a "Likely" human carcinogen based on a Q_1* value assigned to iprodione based on testicular tumors (Leydig Cell) in rats of 4.4×10^{-2} $(mg/kg/day)^{-1}$; was used for assessing cancer risk. Additionally, iprodione has a degradate (3,5-DCA) with an established Q_1*, although that Q_1* value is not relevant to the exposure assessment on the new agricultural uses or the updated residential cancer risk assessment.

Occupational Handler Risk Summary
The occupational handler risk estimates were calculated using the label maximum application rate of 2 lb ai/acre, and assumptions regarding the agricultural equipment and work practices. For non-cancer risk estimates, inhalation and dermal exposures were combined since the endpoints were based on the same effect. For cancer risk estimates, inhalation and dermal exposures are assessed; dermal and inhalation exposures were combined. Based upon the proposed label PPE, non-cancer risk estimates were not of concern at the proposed label PPE. For the private grower scenario, cancer risk estimates range from 1.0×10^{-6} to 1.0×10^{-5} at the proposed label PPE. For the commercial grower scenario, cancer risk estimates range from 6.8×10^{-6} to 3.0×10^{-5} at the proposed label PPE.

Occupational Postapplication Risk Summary
Occupational short- and intermediate-term non-cancer dermal risk estimates were qualitatively assessed for postapplication activities. The proposed use pattern indicates pre-plant and soil

incorporated applications of iprdione. Therefore, the standard "foliar-based" transfer coefficient methodology does not apply. HED believes the proposed soil incorporation is expected to keep exposures low. Based on the Agency's current practices, a quantitative non-cancer occupational postapplication inhalation exposure assessment was not performed for iprodione at this time.

Similarly, a review of the labeled use pattern indicates that because of negligible postapplication worker contact with treated soil, a quantitative postapplication cancer risk assessment is not necessary at this time.

*Restricted Entry Interval***:** Technical iprodione is classified as toxicity category III/IV for acute dermal toxicity, primary eye, and skin irritation. Under the WPS, active ingredients classified as acute toxicity categories III or IV for these exposure routes are assigned a 12-hour restricted entry interval. The proposed product label identifies a 24 hour restricted entry interval for curcurbits and fruiting vegetables.

Residential Exposure

HED assessed residential golf course turf exposure in this assessment in order to complete the aggregate assessment. While the agricultural uses of iprodione for curcurbits and fruiting vegetables are as a nematicide, the golf course use of iprodione assessment is as a fungicide. Iprodione can be applied to golf course turf where there is potential for postapplication residential exposure to golfers. Cancer and non-cancer postapplication risk estimates were calculated for non-occupational postapplication exposure to treated golf course turf. Non-cancer risk estimates for the residential golfer scenario ranged from 3,200 to 4,800; all the risk estimates are above the LOC of 1,000 and therefore, not of concern.

Cancer risk estimates for the golfer scenario range from $3.2x10^{-6}$ to $1.8x10^{-5}$.

Human Studies Review

This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. These data, which include studies from the Pesticide Handlers Exposure Database Version 1.1 (PHED 1.1); the Agricultural Handler Exposure Task Force (AHETF) database, are subject to ethics review pursuant to 40 CFR 26, have received that review, and are compliant with applicable ethics requirements. For certain studies that review may have included review by the Human Studies Review Board. Descriptions of data sources as well as guidance on their use can be found at http://www.epa.gov/pesticides/science/handler-exposure-data.html and http://www.epa.gov/pesticides/science/post-app-exposure-data.html.

Label Recommendation

HED recommends the proposed product label should be modified to clarify that foliar application is prohibited for the proposed new uses on curcurbits and fruiting vegetables. While the crop specific parts of the label indicate clear use directions, other parts of the label appear to allow for aerial application (page 6 and other places) which is contrary to the crop specific curcurbit and fruiting vegetable uses on the proposed label.

1.0 Exposure/Risk Assessment

The registrant requests new uses of iprodione on cucurbits and fruiting vegetables. This memorandum addresses the occupational exposure and risk from this label amendment. HED assessed post-application residential golf course turf exposure in this assessment in order to complete the aggregate assessment.

1.1 Hazard Concerns

Acute Toxicity

The results of acute toxicity testing are given in Table 1.1a. These results indicate that technical iprodione has low to moderate acute toxicity, is a mild eye irritant, and is not a dermal sensitizer.

Table 1.1a. Acute Toxicity of Iprodione

Guideline No.	Study Type	MRID	Results	Toxicity Category
870.1100	Acute Oral –rat	423063-01	LD_{50} = 4468 mg/kg	III
870.1200	Acute Dermal – rabbit	405676-01	LD_{50} > 2000 mg/kg	III
870.1300	Acute Inhalation - rat	429461-01	LC_{50} >5.16 mg/L	IV
870.2400	Primary Eye Irritation – rabbit	418673-01	Mild irritant	III
870.2500	Primary Skin Irritation – rabbit	418673-02	Not an irritant	IV
870.2600	Dermal Sensitization – guinea pig	405676-02 425246-01	Not a dermal sensitizer	N/A

Toxicological PODs Used for Risk Assessment

A summary of the toxicological points of departure (PODs) that are relevant to occupational exposure is included in Table 1.1b.

A single endpoint was selected to cover the dermal and inhalation short- and intermediate-term occupational exposure scenarios. The endpoint for the occupational exposure scenarios was selected from the male rat pubertal assay (MRID 48279201) where the LOAEL is 50 mg/kg/day, based on reduced serum testosterone. The 69 kg bodyweight is appropriate to use for the occupational assessment because the endpoint is an *in utero* effect occurring during prenatal exposure.

HED's level of concern for non-cancer risk estimates is defined by the uncertainty factors that are applied to the assessment. The level of concern for short- and intermediate-term iprodione occupational exposures is 1000, based on the inter- and intra-species factors as well as a 10x uncertainty factor for the lack of a NOAEL in the study.

For the non-cancer residential exposure assessment, the standard inter- and intra-species factors are applicable. Additionally, HED recommends that the 10X FQPA safety factor be retained for the short- and intermediate-term dermal and inhalation exposure points of departure (for the protection of infants and children), based on the LOAEL to NOAEL extrapolation. Therefore the level of concern for residential exposure is an MOE of <1,000.

Based on the available toxicity database and the Agency's current practices, the inhalation risk for iprodione was assessed using an oral study. The toxicity sought expert advice and input on issues related to this route to route extrapolation approach (i.e., the use of oral toxicity studies for inhalation risk assessment) from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009. The Agency received the SAP's final report on March 2, 2010 (http://epa.gov/scipoly/meetings/20091220109meeting.html). The Agency is in the process of evaluating the SAP report and may, as appropriate, re-examine and develop new policies and procedures for conducting inhalation risk assessments, including route to route extrapolation of toxicity data. If any new policies or procedures are developed, the Agency may revisit the need for an inhalation toxicity study for iprodione and/or a re-examination of the inhalation toxicity risk assessment.

In accordance with the EPA Proposed Guidelines for Carcinogen Risk Assessment (April 10, 1996), the Cancer Assessment Review Committee classified Iprodione as a **"likely"** human carcinogen based on the combined hepatocellular adenomas/carcinomas in mice and testicular tumors in male rats with a linear low dose extrapolation approach and a 3/4s interspecies scaling factor for human risk characterization. The CARC determined that for the Leydig cell tumors in male rats, the Q_1* is 4.39×10^{-2} (selected by HED's CARC Committee; TXR 0054534, 3/22/07). HED policy doesn't define a "level of concern" when evaluating cancer risk estimates. The cancer risk estimates are presented based on the Q_1* value for OPP risk managers to evaluate and mitigate as needed.

Table 1.1b. Toxicological PODs for Occupational Exposure Assessment of Iprodione			
Exposure Scenario	Point of Departure (POD)	Uncertainty Factors	Study and Toxicological Effects
Dermal Short-Term (1-30 days) Dermal Intermediate-Term Inhalation Short-Term (1-30 days) Inhalation Intermediate- Term	LOAEL = 50 mg/kg/day Dermal absorption factor = 5% Since no inhalation toxicity data are available, toxicity by the inhalation route is considered to be equivalent to toxicity by the oral route of exposure	UF_A 10x UF_H 10x $UF_{LOAEL \rightarrow NOAEL}$ =10X	Co-critical studies Male pubertal toxicity (rat) MRID 48279201 LOAEL = 50 mg/kg/day, based on significant, dose-related *reductions in serum testosterone levels (↓73%)* Chronic oral toxicity (rat) MRID 42637801/42787001 LOAEL = 12.4 mg/kg/day, based on increases in generalized enlargement of the cells of the zona glomerulosa in males and females, in fine vacuolation of the zona fasciculata and in generalized fine vacuolation of the zone reticularis in males in the adrenal cortex, an increased incidence of interstitial cell hyperplasia, reduced spermatozoa in the epididymides, reduced secretion of the seminal vesicles, increased hemosiderosis in the spleen in females, and increased liver weight. NOAEL = 6.1 mg/kg/day
Inhalation Short-Term (1-30 days) Inhalation Intermediate- Term	LOAEL = 50 mg/kg/day	UF_A 10x UF_H 10x $UF_{LOAEL \rightarrow NOAEL}$ =10X	Male pubertal assay (rat) MRID 48279201 LOAEL = 50 mg/kg/day, based on reduced serum testosterone levels
Dermal Absorption Factor	5 percent of the oral dose		Based on the value measured at 10 hours in a dermal absorption study (MRID 43535003).
Carcinogenicity	$Q_1^* = 4.4 \times 10^{-2}$ $(mg/kg/day)^{-1}$		Iprodione is classified as a "Likely" human carcinogen, based on findings in the Rat Leydig cells (CARC-based Q1*)

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. LOAEL = lowest observable adverse effect level. UF = uncertainty factor. UFA = extrapolation from animal to human (interspecies).

1.2 Proposed Use Profile

The proposed new uses for the product Enclosure™ 4 Flowable, a liquid concentrate formulation (41.6% iprodione; 4 lbs ai per gallon), are on cucurbits and fruiting vegetables. The maximum application rate allowed on this label for cucurbits and fruiting vegetables is 4 pints of Enclosure™ 4 Flowable per acre (2 lb ai/acre) per application and up to 3 applications are

allowed per season. The maximum application rate per season is 6 pints per acre (3 lb ai/A/season). The pre-harvest interval (PHI) for cucurbits and fruiting vegetables is 14 days (the final application can be made up to 14 days before harvest). Application consists of a soil directed pre-plant or post-plant mechanical incorporation. The application timings and methods are described below.

Cucurbits and fruiting vegetables, transplanted crops: The application is specified to be a preplant and post plant soil treatment. For transplanted crops, the label specifies that the 1st application should be made 4-7 days prior to transplant and that the product should be thoroughly incorporated (mechanically or through drip irrigation) into the bed at least 3-5 inches deep. The 2nd application is specified to be made through drip chemigation 7- 10 days after transplanting. The 3rd application is specified to be made through drip chemigation 12-14 days after the 2nd application.

Cucurbits and fruiting vegetables, seeded crops: The application is specified to be a pre plant and post plant soil treatment. For seeded crops, the label specifies that the 1st application be made 4-7 days prior to seeding. The product should be thoroughly incorporated (mechanically or through drip chemigation) into the bed at least 3-5 inches. The 2nd application is specified to be made through drip chemigation 10-14 days after seedling emergence. The 3rd application is specified to be made through drip chemigation 12-14 days after the 2nd application.

The label specifies that for nematode supplemental control, the product should be applied through drip chemigation 14-21 days after transplanting, and that subsequent applications through drip chemigation should be made on 14-day intervals.

The label specifies that when the high rate of 4 pints per acre is used, only one subsequent application at 2 pints per acre is allowed. This application should be made 7-10 days after transplanting or 10-14 days after seedling emergence.

1.3 Existing Use Profile for Golf Course Turf

HED conducted a cancer risk assessment based on non-occupational exposure to treated golf course turf to contribute an aggregate human health risk assessment. A variety of existing product labels for turf were reviewed. Because iprodione can be used to prevent disease or to control disease infestation, product labels indicate a range of potential application rates depending on seasonality or disease pressure. Some product labels have differential application rates for golf course greens and fairways. For example, 9198-229 indicates an application rate of 8.2 and 5.5 lbs ai/A for tees and greens and fairways, respectively. Granular formulations are to be applied using a light rate (1.4 lb ai/acre) to prevent certain fungi such as pink or gray snow mold or leaf spot. Other liquid product labels indicate a normal (2.7 lb ai/acre) to heavy application rate (4.1 lb ai/acre) to control fungi such as leaf spot, brown patch and red leaf spot (representative label: EPA Reg. No. 538-159).

2.0 Occupational Exposures and Risk Estimates

HED uses the term handlers to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct job functions or tasks related to applications and exposures can vary depending on the specifics of each task. Job requirements (amount of chemical used in each application), the kinds of equipment used, the target being treated, and the level of protection used by a handler can cause exposure levels to differ in a manner specific to each application event.

Tasks associated with occupational pesticide handlers are categorized using one of the following terms:

- Mixers and/or Loaders: these individuals perform tasks in preparation for an application. For example, mixers/loaders would mix and prepare the nematicide product prior to application.
- Applicators: these individuals are involved in the pesticide application process (they do job functions related to a pesticide application event). These individuals would complete the product application.

The following occupational handler exposure scenarios were assessed:

1 – Mix/Load Liquid for Chemigation
2 – Mix/Load Liquid for Groundboom Application
3 – Apply spray by Groundboom Sprayer

A chemical can produce different effects based on how long a person is exposed, how frequently exposures occur, and the level of exposure. HED classifies exposures from 1 to 30 days as short-term and exposures 30 days to six months as intermediate-term. HED completes both short- and intermediate-term assessments for occupational scenarios in all cases because these kinds of exposures are likely and acceptable use/usage data are not available to justify deleting intermediate-term scenarios. Based on use data and label instructions, HED believes that occupational exposures may occur over a single day or up to weeks at a time for many use-patterns and that intermittent exposure over several weeks may also occur. Some applicators may apply these products over a period of weeks, because they are commercial applicators who are completing multiple applications for multiple clients. Long-term (greater than six months) handler exposures are not expected for iprodione based on the proposed use pattern.

Occupational handler exposure assessments are completed by HED using different levels of risk mitigation. Typically, HED uses a tiered approach evaluating various levels of personal protective equipment. This approach is used to ensure that the lowest level of risk mitigation that provides adequate protection is selected, since the addition of PPE and engineering controls involves an additional expense to the user and (in the case of PPE) also involves an additional burden to the user due to decreased comfort and dexterity and increased heat stress and respiratory stress.

2.1 Occupational Handler Exposure Data

It is the policy of HED to use the best available data to assess handler exposure. Sources of generic handler data, used as surrogate data in the absence of chemical-specific data, include the Pesticide Handlers Exposure Database Version 1.1 (PHED 1.1), the Agricultural Handler Exposure Task Force (AHETF) database, the Outdoor Residential Exposure Task Force (ORETF) database, or other registrant-submitted occupational exposure studies. Some of these data are proprietary (e.g., AHETF data), and subject to the data protection provisions of FIFRA. The standard values recommended for use in predicting handler exposure that are used in this assessment, known as "unit exposures", are outlined in the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (http://www.epa.gov/opp00001/science/handler-exposure-table.pdf), which, along with additional information on HED policy on use of surrogate data, including descriptions of the various sources, can be found at http://www.epa.gov/pesticides/science/handler-exposure-data.html.

The appropriate unit exposure data are listed below in Table 2.1.

Table 2.1. Iprodione Occupational Handler Dermal and Inhalation Unit Exposures used for Non-Cancer and Cancer Risk Assessments

Exposure Scenario	Dermal Unit Exposure (mg/ lb ai)				Inhalation Unit Exposure (mg/ lb ai)			
	Baseline[A]	Single Layer plus Gloves[B]	Double Layer Plus Gloves[C]	Engineering Control[D]	Baseline[E]	PF5 Respirator	PF10 Respirator	Engineering Control[F]
Mixer/Loader Scenarios								
Mixing/Loading Liquids for Chemigation Application	0.22	0.0376	0.0291	Closed System: 0.0086	0.000219	0.000044	0.000022	Closed System: 0.000083
Mixing/Loading Liquids for Groundboom Application	0.22	0.0376	0.0291	Closed System: 0.0086	0.000219	0.000044	0.000022	Closed System: 0.000083
Applicator Scenarios								
Applying Spray via Open Cab Groundboom	0.0786	0.0161	0.0126	Enclosed Cab: 0.0051	0.00034	0.00007	0.00003	Enclosed Cab: 0.000043

A. Baseline dermal unit exposures represent long pants, long sleeved shirts, shoes, and socks, no gloves.
B. Single Layer plus gloves (minimum PPE) dermal unit exposure represent long pants, long sleeved shirts, shoes, socks and chemical-resistant gloves.
C. Double layer plus gloves (Maximum PPE) dermal unit exposure represent long pants, long sleeved shirt, shoes, socks, coveralls, and chemical resistant gloves.
D. Engineering control includes closed mixing and loading for mixer/loaders and an enclosed cab for applicators.
E. Baseline inhalation unit exposures represent no respirator protection (baseline).
F. Engineering control includes closed mixing and loading for mixer/loaders and an enclosed cab for applicators.

2.2 Occupational Handler Non-Cancer Risk Estimates

2.2.1 Occupational Handler Exposure and Non-Cancer Risk Assumptions

The assumptions and factors used in the risk calculations include:

- The application rate is 2 lbs ai per acre [proposed curcurbit/vegetable use].

- Unit exposure data are outlined above in Table 2.1.
- The area treated per day is 350 acres for chemigation application short/intermediate-term exposures and 80 acres for groundboom application short/intermediate-term exposures. These values were derived from ExpoSAC policy 3.1.
- The body weight for short- and intermediate-term non-cancer exposure assessment is 69 kg because the effects are based on developmental effects.

2.2.2 Occupational Handler Non-Cancer Risk Estimate Calculations

Average Daily Dose (ADD): Potential daily exposures for occupational handlers were calculated using the following formula:

Daily Exposure (mg ai /day) = UE (mg ai / lb ai) * AR (lb ai /A) * AT (A /day)

Where:
UE = Unit Exposure (from PHED),
AR = maximum application rate according to proposed label, and
AT = daily acres treated.

The daily doses were calculated using the following formula:

$$\text{Average Daily Dose (mg ai/kg/day)} = \frac{[\text{Daily Exposure (mg ai/day)} * \text{Absorption (\%)}]}{\text{Body Weight (kg)}}$$

Margin of Exposure: Non-cancer inhalation risk estimates for each application handler scenario are calculated using a Margin of Exposure (MOE), which is a ratio of the toxicological endpoint to the daily dose of concern. Risk estimates were calculated for inhalation exposure, as there was no dermal endpoint.

MOE = PoD (typically a NOAEL or LOAEL in mg/kg/day) / ADD (mg/kg/day)

Where:
MOE = Margin of Exposure: value used by HED to represent risk or risk estimates (unitless),
PoD = Point of Departure,
NOAEL = No Observed Adverse Effect Level: Dose level in a toxicity study,
LOAEL = Lowest Observed Adverse Effect Level; and
ADD = Average Daily Dose: the absorbed dose received from exposure to a pesticide in a given scenario.

A combined dermal and inhalation MOE was calculated to show combined dermal and inhalation risk estimates. Combined risks of concern are identified by an MOE < 1000.

$$\text{Combined MOE} = \frac{\text{Dermal and Inhalation PoD (typically a NOAEL/LOAEL in mg/kg/day)}}{\text{Dermal ADD (mg/kg/day)} + \text{Inhalation ADD (mg/kg/day)}}$$

Where:

MOE	= Margin of Exposure: value used by HED to represent risk or risk estimates (unitless),
PoD	= Point of Departure,
NOAEL	= No Observed Adverse Effect Level (mg/kg/day): Dose level in a toxicity study, where no observed adverse effects occurred in the study, and

ADD = Average Daily Dose (mg/kg/day): the absorbed dose received from exposure to a pesticide in a given scenario.

2.2.3 Occupational Handler Non-Cancer Risk Estimates

The occupational handler non-cancer risk estimates are included in Table 2.2.3. Combined MOEs for the handler non-cancer risk estimates exceed the level of concern of 1000 with the proposed label personal protective equipment (i.e., gloves, no respirator), which means that the non-cancer risk estimates are not of concern to HED.

Table 4.1.1. Short- and Intermediate-term Exposure & Risk to Occupational Handlers For Iprodione Proposed New Use Sites.						
Crop or Target	**Unit Exposure[1] (mg ai/lb handled)**	**Applic. Rate[2] (lb ai/A)**	**Units Treated[3] (A/day)**	**Avg. Daily Dose[4] (mg ai/kg /day)**	**MOE[4]**	**Combined MOEs[4]**
Mixer/Loader –Liquids –Chemigation Applications						
Fruiting vegetables/curcurbits	Dermal Baseline: 0.220 PPE-G: 0.0376	2	350	Dermal Baseline: 0.39 PPE-G: 0.067	Dermal Baseline: **450** PPE-G: 2,600	Baseline dermal + inhalation: **440** PPE-G dermal + Baseline inhalation: 2,600
	Inhal. Baseline: 0.000219			Inhal. Baseline: 0.00077	Inhal. Baseline: 23,000	
Mixer/Loader –Liquids –Groundboom Applications						
Fruiting vegetables/curcurbits	Dermal Baseline: 0.220	2	80	Dermal Baseline: 0.09	Dermal Baseline: 2,000	Baseline dermal + inhalation: 1900 PPE-G dermal + Baseline inhalation: 11,000
	Inhal. Baseline: 0.000219			Inhal: Baseline: 0.00018	Inhal. Baseline: 98,000	
Applying Sprays via Groundboom Equipment						
Fruiting vegetables/curcurbits	Dermal Baseline: 0.0786	2	80	Dermal Baseline: 0.032	Dermal Baseline: 9,000	Baseline dermal + inhalation: 1,900
	Inhal. Baseline: 0.00034			Inhal. Baseline: 0.00027	Inhal. Baseline: 14,000	
	Inhal. Baseline: 0.00035			Inhal. Baseline: 0.0012	Inhal. Baseline: 5,500	

1. See Section 2.1 for additional information
2. See Section 1.2 for additional information
3. See Section 2.2.1 for additional information
4. See Section 2.2.2 for additional information

2.3 Occupational Handler Cancer Risk Estimates

2.3.1 Occupational Handler Exposure and Cancer Risk Assumptions

The assumptions and factors used in the risk calculations include:

- The application rate is 2 lbs ai per acre [proposed curcurbit/vegetable use].
- The area treated per day is 350 acres for chemigation application and 80 acres for groundboom application. These values were derived from ExpoSAC policy 3.1.
- To calculate cancer risk estimates, it is assumed that private growers would be exposed 10 days per year and commercial applicators would be exposed 30 days per year. It is assumed that handlers would be exposed for 35 years out of a 70 year lifespan.
- The body weight for cancer risk calculations is 80 kg (average bodyweight for U.S. adults)
- A 5% dermal absorption factor is used for the handler cancer assessment

2.3.2 Occupational Handler Cancer Risk Calculations

EPA conducted an assessment of the carcinogenic risk estimates associated with iprodione following exposures to occupational handlers.

The occupational handler exposure and cancer risk calculations are presented in this section. Cancer risk estimates were calculated using a linear low-dose extrapolation approach in which a Lifetime Average Daily Dose (LADD) is first calculated and then compared with a Q_1* that has been calculated for iprodione based on dose response data in the appropriate toxicology study ($0.044\ (mg/kg/day)^{-1}$). Absorbed average daily dose (ADD) levels were used as the basis for calculating the LADD values. Dermal and inhalation ADD values were first added together to obtain combined ADD values. LADD values were then calculated and compared to the Q_1* to obtain cancer risk estimates.

Lifetime Average Daily Dose: After the development of the ADD values, the next step required to calculate the carcinogenic risk is to amortize these values over the working lifetime of occupational handlers based on use patterns, which results in the LADD for that use. LADD values were calculated using the following equation:

$$LADD = ADD \times \frac{\text{Treatment Frequency}}{\text{365 days/year}} \times \frac{\text{Working Duration}}{\text{Lifetime}}$$

Where:
Lifetime Average Daily Dose = the amount as absorbed dose received from exposure to a pesticide in a given scenario over a lifetime (mg pesticide active ingredient/kg body weight/day, also referred to as LADD),
Average Daily Dose = the amount as absorbed dose received from exposure to a pesticide in a given scenario on a daily basis (mg pesticide active ingredient/kg body weight/day, also referred to as ADD),
Treatment Frequency = the annual frequency of an application by an individual (days/year),
Working Duration = the amount of a lifetime that an individual spends engaged in a career involving pesticide exposure (35 years), and

Lifetime = the average life expectancy of an individual (78 years).

Cancer Risk Estimates: Cancer risk calculations were completed by comparing the LADD values calculated above to the Q_1* values for iprodione (Q_1* = 0.044 $(mg/kg/day)^{-1}$). The Agency considered more typical users in these calculations (i.e., private growers at 10 events per year) as well as more frequent users that might represent commercial applicators (i.e., 30 events per year). Cancer risk values were calculated using the following equation:

Total Risk = (Dermal LADD + Inhalation LADD) x Q_1*

Where:
Risk = Probability of excess cancer cases over a lifetime (unitless),
Dermal Lifetime Average Daily Dose = the amount as absorbed dose received from dermal exposure to a pesticide in a given scenario over a lifetime (mg pesticide active ingredient/kg body weight/day, also referred to as LADD),
Inhalation Lifetime Average Daily Dose = the amount as absorbed dose received from inhalation exposure to a pesticide in a given scenario over a lifetime (mg pesticide active ingredient/kg body weight/day, also referred to as LADD), and
Q_1* = Quantitative dose response factor used for linear, low-dose response cancer risk calculations $(mg/kg/day)^{-1}$.

For this assessment, cancer risk estimates were calculated at the proposed label PPE for occupational handlers and then with increasing tiers of personal protective equipment for review by the risk manager.

2.3.3 Occupational Handler Cancer Risk Estimates

All of the cancer risk calculations for occupational iprodione handlers completed in this assessment are included in Tables 2.3.3a and 2.3.3b. The specifics of each table and a brief summary of results are provided below.

- Table 2.3.3: Iprodione Occupational Handler Cancer Risk Estimates for Private Growers: Presents cancer risk estimates for combined dermal and inhalation for private growers (i.e., 10 applications per year) with each possible combination of dermal and respiratory protection considered in this assessment.
- Table 2.3.4: Iprodione Occupational Handler Cancer Risk Estimates for Commercial Applicators: Presents cancer risk estimates for combined dermal and inhalation for commercial applicators (i.e., 30 applications per year) with each possible combination of dermal and respiratory protection considered in this assessment.

The LADD values were applied to the Q_1* value to calculate the cancer risk estimates as described above. Cancer risk estimates were calculated for different exposure scenarios at different levels of personal protective equipment. For the private grower scenario, cancer risk estimates range from 1.0×10^{-6} to 1.0×10^{-6} at the proposed label PPE. For the commercial grower scenario, cancer risk estimates range from 6.8×10^{-6} to 3.0×10^{-5} at the proposed label PPE.

The proposed label requires that mixer/loaders wear long-sleeve shirt and long pants, chemical resistant gloves, chemical resistant footwear plus socks, and a chemical resistant apron (single layer plus gloves and no respirator). The label requires applicators using mechanical ground

equipment wear long-sleeve shirt and long pants and shoes plus socks (single layer, no gloves and no respiratory protection).

Table 2.3.3. Iprodione Occupational Handler Cancer Risk Estimates - Private Grower

Exposure Scenario	Amount of Ai Applied per Day	PPE	Total Average Daily Dose[A] (mg/kg/day)	Lifetime Average Daily Dose[B] (mg/kg/day)	Cancer Risk[C] $Q1^*=0.044$ $mg/kg/day^{-1}$
Mixer/ Loader Scenarios					
Mix/Load Liquid for Chemigation	2 lb ai/acre X 350 acres/day = 700 lb ai/day	Dermal – Double Layer Gloves Inhalation – Baseline	0.017	0.00023	$1.0x\ 10^{-5}$ (required label PPE)
		Dermal – Double Layer Gloves Inhalation – PF5 Respirator	0.01455	0.0002	9.0×10^{-6}
		Dermal – Double Layer Gloves Inhalation – PF10 Respirator	0.019	0.00026	$1.1x\ 10^{-5}$
Mix/Load Liquid for Groundboom Application	2 lb ai/acre X 80 acres/day = 160 lb ai/day	Dermal – Double Layer Gloves Inhalation – Baseline	0.0033	0.000052	$1.0x\ 10^{-6}$ (required label PPE)
		Dermal – Double Layer Gloves Inhalation – PF5 Respirator	0.0034	0.000047	7.6×10^{-7}
		Dermal – Double Layer Gloves Inhalation – PF10 Respirator	0.0034	0.000059	7.1×10^{-7}
Applicator Scenarios					
Apply Spray by Open Cab Groundboom	2 lb ai/acre X 80 acres/day = 160 lb ai/day	Dermal – Baseline Inhalation – Baseline	0.0098	1.3E-04	4.6×10^{-6} (required label PPE)

A. Dermal dose (mg/kg/day) = [unit exposure (mg/lb ai) * lb ai handled per day * Dermal absorption factor (0.05))] / BW (80 kg)
Inhalation dose (mg/kg/day) = [unit exposure (mg/lb ai) * lb ai handled per day)] / BW (80 kg)
Total average daily dose (mg/kg/day) = dermal dose (mg/kg/day) + inhalation dose (mg/kg/day)
B. Lifetime Average daily dose (mg/kg/day) = Total Average Daily Dose * (10 days for private grower/ 365 days) * (35 years/80 years)
C. Cancer Risk = Lifetime Average Daily Dose (mg/kg/day) * Q_1*(0.044 $mg/kg/day^{-1}$)

Table 2.3.4. Iprodione Occupational Handler Cancer Risk Estimates - Commercial Grower					
Exposure Scenario	**Amount of Ai Applied per Day**	**PPE**	**Total Average Daily Dose[A] (mg/kg/day)**	**Lifetime Average Daily Dose[B] (mg/kg/day)**	**Cancer Risk[C] Q1*=0.044 mg/kg/day^{-1}**
Mixer/ Loader Scenarios					
Mix/Load Liquid for Chemigation/ Aerial Application	2 lb ai/acre X 350 acres/day = 700 lb ai/day	Dermal – Double Layer Gloves Inhalation – Baseline	0.017	0.00069	3.0×10^{-5} (required label PPE)
		Dermal – Double Layer Gloves Inhalation – PF5 Respirator	0.015	0.00061	2.7×10^{-5}
		Dermal – Double Layer Gloves Inhalation – PF10 Respirator	0.019	0.00061	2.4×10^{-5}
Mix/Load Liquid for Groundboom Application	2 lb ai/acre X 80 acres/day = 160 lb ai/day	Dermal – Double Layer Gloves Inhalation – Baseline	0.0038	0.00016	6.8×10^{-6} (required label PPE)
		Dermal – Double Layer Gloves Inhalation – PF5 Respirator	0.0034	0.00014	6.2×10^{-6}
		Dermal – Double Layer Gloves Inhalation – PF10 Respirator	0.0034	0.00014	6.2×10^{-6}
Applicator Scenarios					
Apply Spray by Open Cab Groundboom	2 lb ai/acre X 80 acres/day = 160 lb ai/day	Dermal – Baseline Inhalation – Baseline	0.0098	4.0E-04	1.4×10^{-5} (required label PPE)

A. Dermal dose (mg/kg/day) = [unit exposure (mg/lb ai) * lb ai handled per day * Dermal absorption factor (0.05))] / BW (80 kg)
Inhalation dose (mg/kg/day) = [unit exposure (mg/lb ai) * lb ai handled per day)] / BW (80 kg)
Total average daily dose (mg/kg/day) = dermal dose (mg/kg/day) + inhalation dose (mg/kg/day)
B. Lifetime Average daily dose (mg/kg/day) = Total Average Daily Dose * (30 days for private grower/ 365 days) * (35 years/78 years)
C. Cancer Risk = Lifetime Average Daily Dose (mg/kg/day) * Q_1*(0.044 mg/kg/day^{-1})

3.0 Occupational Postapplication Exposures and Risk Estimates

HED uses the term post-application to describe exposures that occur when individuals are present in an environment that has been previously treated with a pesticide (also referred to as re-entry exposure). Such exposures may occur when workers enter previously treated areas to perform job functions, including activities related to crop production, such as scouting for pests or harvesting. Post-application exposure levels vary over time and depend on such things as the type of activity, the nature of the crop or target that was treated, the type of pesticide application, and the chemical's degradation properties. In addition, the timing of pesticide applications, relative to harvest activities, can greatly reduce the potential for postapplication exposure.

Post-application exposures to the proposed iprodione uses on curcurbits and fruiting vegetables uses have not been assessed in this document as the exposure potential is low. The proposed label is for chemigation/soil incorporation applications that are watered in to the top 3-5 inches of soil. In cases like iprodione where the proposed uses do not follow the standard "foliar-based" transfer coefficient methodology, exposure assessors reference ExpoSAC policy 3.1 on guidance on crop-activity combinations utilizing an alternate transfer coefficient method.

Due to the method and timing of applications and typical agricultural practices for these crops, HED has determined that a specific post-application exposure assessment is not necessary for these scenarios. This determination is based on the following: (1) routine hand labor activities that involve significant contact with the treated soil/planting medium are not required, or are not required for several weeks or months after the application, and (2) reentry activities that may be necessary are likely to result in relatively low levels of dermal exposure because contact with the treated medium (soil) is minimal or infrequent.

3.1 Occupational Postapplication Exposure and Non-Cancer Risk Estimates

Occupational Postapplication Dermal Exposure

Based on a review of the non-cancer hazard database, HED believes that the potential for dermal postapplication worker exposure is low, provided at least a 12-hour restricted entry interval (REI) and other proposed restrictions based on worker reentry are observed.

As noted above, the proposed use pattern is for soil directed/soil-incorporated applications of iprodione and thus no foliage will be contacted. Additionally, reentry activities that may be necessary are likely to result in negligible dermal exposure because contact with the treated medium is infrequent.

Occupational Postapplication Inhalation Exposure

Based on the Agency's current practices, a quantitative postapplication inhalation exposure assessment was not performed for iprodione at this time primarily because it has a low vapor

pressure (3.8×10^{-9} mm Hg[1]). However, volatilization of pesticides may be a potential source of post-application inhalation exposure to individuals nearby to pesticide applications. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009. The Agency received the SAP's final report on March 2, 2010 (http://www.epa.gov/scipoly/SAP/meetings/2009/120109meeting.html). The Agency is in the process of evaluating the SAP report and may, as appropriate, develop policies and procedures to identify the need for and, subsequently, the way to incorporate postapplication inhalation exposure into the Agency's risk assessments. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative postapplication inhalation exposure assessment for iprodione.

Although a quantitative postapplication inhalation exposure assessment was not performed, an inhalation exposure assessment was performed for occupational/commercial handlers. Handler exposure resulting from application of pesticides outdoors is likely to result in higher exposure than postapplication exposure. Therefore, it is expected that these handler inhalation exposure estimates would be protective of most occupational postapplication inhalation exposure scenarios.

3.2 Occupational Postapplication Cancer Risk Estimates

3.2.1 Occupational Postapplication Exposure and Cancer Risk Assumptions

HED typically assesses dermal postapplication exposure potential for field workers, for both non-cancer and cancer assessments (when a Q_1* has been determined). HED has identified a Q_1* for the parent compound and one Q_1* from a iprodione degradate. However, because of review of the proposed label and proposed use pattern, HED has determined that a quantitative post-application exposure assessment is not necessary for these scenarios. The determination is based on the exposure potential (similar to the non-cancer exposure potential characterization identified above in section 3.0) for the parent compound.

While there is an additional Q_1* value for a degradate of iprodione (3,5-DCA[2]); no quantitative postapplication cancer assessment has been completed for the degradate. The proposed label for fruiting vegetables and curcurbits directs applicators to pre-emergent soil incorporation or post-emergent soil directed sprays. Therefore, there is negligible occupational postapplication dermal potential for the parent compound, and no post-application dermal exposure potential for the 3,5-DCA degradate.

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[1] http://www.oehha.org/multimedia/biomon/pdf/0709iprodione.pdf

[2] 3, 5-DCA is not a registered pesticide; therefore, there are no FIFRA toxicology data for this compound. In the past, HED has used the Q1 * for p-chloroaniline (PCA) to assess the carcinogenic risk for other structurally related chloroanilines. The HED policy on chloroanilines specifies that chloroaniline metabolites should be considered to be toxicologically equivalent to PCA unless there is sufficient evidence that the metabolite is not carcinogenic. A Q_1 * of 6.38×10^{-2} $(mg/kg/day)^{-1}$ in human equivalents has been calculated for p-chloroaniline. This Q_1* is based on the spleen sarcoma rate in male rats from an NTP bioasssay, linearized low dose multistage model, and the 3/4s interspecies body scaling factor.

4.0 Residential Exposure

According to the 1998 reregistration eligibility decision (RED) for iprodione, "Based on cancer risk concerns, the Agency has determined that iprodione residential uses on turf, ornamentals and vegetable/small fruit gardens are ineligible for reregistration. The registrant [at the time of the RED], Rhone-Poulenc, has requested to voluntary cancelation of all residential uses of iprodione." Therefore, residential turf uses of iprodione are no longer registered by the Agency. However, there are iprodione-based products that can be professionally applied to golf courses, where there is potential for non-occupational postapplication exposure to golfers.

This "golfer" scenario is assessed in this document to update the residential exposure assessment and to be used in the updated aggregate exposure assessment. While the agricultural uses of iprodione for curcurbits and fruiting vegetables are as a nematicide, HED calculated risk estimates for exposure to treated golf course turf to include in the aggregate risk assessment.

4.1 Residential Handler Exposure

There are no registered residential products that can be applied by residential handlers; therefore, residential handler exposure has not been quantitatively assessed.

4.2 Use of TTR Data for Iprodione Post-application Exposure Assessments

This assessment contains potentially compensable turf transferable residue data generated by Rhône-Poulenc. The transferable turf residue (TTR) data are available and scientifically sound for risk assessment (MRID 44968001; reviewed by HED in D389183). The data set measured TTR in 3 locations; Georgia, New York, and California. As data are available, HED evaluated cancer risk estimates based on the potential exposure the highest 14 day average TTR value; from the California-based measurements.

There are TTR data available for iprodione (MRID 44968001) and a summary is included in Appendix A. Six applications of 5.45 lb iprodione/A in flowable concentrate formulation were applied by groundboom in three test sites, GA, CA, and NY. For the residential exposure assessment, the predicted TTR values from the California site were used for 14- and 28-day averaging to provide a health protective assessment of potential exposure to iprodione parent residues. Table 4.3.1 details the TTR values used for the residential exposure assessment.

Calculations of non-cancer postapplication exposures are typically completed using maximum application rates identified in the label and "day 0" residue values. In this case, the risk estimates are also shown for the highest TTR residue value as a screening level assessment. The maximum application rate for products applied to golf courses is 5.5 lb ai/A; therefore the available TTR data did not need to be adjusted based on the application rate. Calculations of cancer post-application exposures are completed using average application rates (2.5 lbs ai/A) identified on product labels to reflect lifetime exposure potential. The available TTR data was adjusted to reflect that application rate.

Table 4.3.1: Use of TTR data Derived from MRID 44968001				
Postapplication Exposure Assessment Type	**TTR value used (in ug/cm^2)**	**Application Rate**	**Averaging time**	**Site Location**
Non-Cancer Assessment	0.49	Maximum (5.5 lb ai/A)	14 day	California
Cancer Assessment	0.22	Average (2.5 lb ai/A)	14 day	California
	0.15	average (2.5 lb ai/A)	28 day	California
Upper bound Cancer Assessment[1]	Greens -1.98 Fairways - 0.49	Maximum (20/5.5 lb ai/A)2	14 day	California
	Greens -1.98 Fairways - 0.49	Maximum (20/5.5 lb ai/A)2	28 day	California

1) The upper bound cancer risk assessment reflects a weighted average of residue exposure from time spent on fairways vs. greens & maximum application rates
2) Weighted average application rate

4.3 Residential Postapplication Exposure and Non-cancer Risk Estimates

Residential Post-application Dermal Exposure

This action covers the new uses of iprodione on fruiting vegetables and curcurbits. However, this document includes qualitative and quantitative exposure assessments for the residential postapplication "golfer" scenarios because a revised aggregate assessment is needed to complete this iprodione action.

Iprodione residential post-application scenarios include individuals playing golf on treated turf. As a result, HED's Standard Operating Procedures (SOP's) for Residential Exposure Assessments, (2012), as well as chemical-specific residue data from a turf transferable residue (TTR) study (MRID 44968001) are used to assess residential golfer exposure. The 2012 residential SOP's outline quanitatively assessing exposure to the following lifestages: 1) adults, 2) 11 to < 16 year olds, and 3) 6 to < 11 year olds.

4.3.1 Non-Cancer Dermal Post-application Exposure

This scenario assumes that pesticide residues are transferred to the skin of individuals that enter treated areas for recreation or other activities such as golfing. Below are some assumptions about the dermal exposure potential.

Assumptions:

- Residential post-application exposure must be assessed on the same day the pesticide is

applied since it is assumed that golfers could be exposed to turf grass immediately after application. Therefore, exposures are based on "day 0" residues.

- TTR value is assumed to be 0.682 ug/cm^2 based on predicted day 0 residue value calculated by a first-order dissipation kinetics and decay model from chemical-specific data. A summary of the TTR study is presented in section 4.2 of this document. The full study review is available (D389183). An upper bound TTR residue value was used as a screening level assessment.
- Transfer coefficients (TCs) were used to assess dermal exposure resulting from golfing.
- An average body weight of 69 kg was used to assess dermal exposure for adults. Body weights of 57 and 32 were used to assess dermal exposure for 11 to < 16 yrs and 6 to < 11 yrs old, respectively. Those bodyweights reflect average bodyweights for those age groups.
- Duration of exposure on golf course lawns, greens and tees is assumed to be 4 hours.

Equations:

Dermal Dose (mg/kg/day) = [TTR (µg/cm^2) x 0.001 (mg/µg) x TC (cm^2/hr) x ET (hr/day)]/BW (kg)

Where:

Dose = Dermal exposure on day of application attributable for activity in a previously treated area (mg/kg/day);
TTR = Turf Transferable Residue (µg/cm^2);
TC = Transfer Coefficient (cm^2/hr);
ET = Exposure Time (hours); and,
BW = Body Weight (kg).

Dermal MOE = LOAEL (mg/kg/day)/Dermal Dose (mg/kg/day)

Post-application Dermal Exposure and Risk Estimate

Short-term dermal post-application exposure and risk estimates for golfers resulted in MOEs greater than the LOC and therefore are not of concern to HED. A summary of the residential short-term dermal exposures is shown below in Table 4.2.1. Risk estimates are presented with the highest predicted residue values and the predicted "day 0" residue values; neither present risk estimates of concern based on the level of concern of 1,000.

Table 4.2.1. Post-application Short-term Dermal Exposure and Risk Estimates for Iprodione.

Scenario	Application Rate (lb ai/A)	TTR [1] (µg/cm^2)	CF	TC [2] (cm^2/hr)	ET (hrs)	BW (kg)	Dose [3] (mg/kg/day)	Dermal MOE [4]
Golfer								
Adult	5.5	0.682	0.001	5,300	4	69	0.010	4,800
11 to < 16 yrs old	5.5	0.682	0.001	4,400	4	57	0.011	4,700
6 to < 11 yrs old	5.5	0.682	0.001	2,900	4	32	0.012	4,000
Adult	5.5	0.85	0.001	5,300	4	69	0.013	3,800
11 to < 16 yrs old	5.5	0.85	0.001	4,400	4	57	0.013	3,800

Table 4.2.1. Post-application Short-term Dermal Exposure and Risk Estimates for Iprodione.								
Scenario	**Application Rate (lb ai/A)**	**TTR [1] (µg/cm^2)**	**CF**	**TC [2] (cm^2/hr)**	**ET (hrs)**	**BW (kg)**	**Dose [3] (mg/kg/day)**	**Dermal MOE [4]**
6 to < 11 yrs old	5.5	0.85	0.001	2,900	4	32	0.015	3,200

1. Turf Transferable Residues (TTR) = 0.682 ug/cm^2 is based on predicted day 0 residue value calculated from chemical-specific data (MRID No. 44968001). 0.85 ug/cm^2 is the highest predicted residue value run as a screening level assessment.
2. Transfer Coefficients are derived from HED's "Science Advisory Council for Exposure (ExpoSAC) Policy 3- Revised March 2012"
3. Dermal Dose (mg/kg/day) = [TTR (µg/cm^2) x 0.001 (mg/µg) x TC (cm^2/hr) x ET (hr/day)]/ BW (kg).
4. Dermal MOE = LOAEL (50 mg/kg/day)/Dermal Dose (mg/kg/day).

Spray Drift

Spray drift is a potential source of exposure for residents living in close proximity to spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential source of exposure from the ground application method employed for iprodione. The Agency has been working with the Spray Drift Task Force (a membership of US pesticide registrants), EPA Regional Offices, State Lead Agencies for pesticide regulation, and other parties to develop the best spray drift management practices. The Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed its evaluation of the new database submitted by the Spray Drift Task Force, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard airblast, and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift with specific products with significant risk estimates associated with drift.

Residential Postapplication/Bystander Inhalation Exposure

Based on the Agency's current practices, a quantitative postapplication inhalation exposure assessment was not performed for iprodione at this time. However, volatilization of pesticides may be a potential source of postapplication inhalation exposure to individuals nearby to pesticide applications. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009. The Agency received the SAP's final report on March 2, 2010 (http://www.epa.gov/scipoly/SAP/meetings/2009/120109meeting.html). The Agency is in the process of evaluating the SAP report and may, as appropriate, developing policies and procedures, to identifying the need for and, subsequently, the way to incorporate postapplication inhalation exposure into the Agency's risk assessments. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative postapplication inhalation exposure assessment for iprodione.

4.4 Residential Postapplication Exposure and Cancer Risk Estimates

There are currently registered products that can be professionally applied to golf courses, where there is potential for postapplication residential exposure to golfers. This scenario is assessed in this document to update the residential exposure assessment and to be used in the updated aggregate exposure assessment.

HED calculates cancer risk estimates for adults exposed to pesticide products during recreational activities. In this case, pesticide products containing iprodione can be applied commercially to golf courses, and recreational golfers can be exposed to those residues. Adult cancer risk estimates were calculated from golfer exposure to previously treated golf course turf. HED expects dermal exposure is the primary exposure route for adults exposed through recreational golf.

The postapplication cancer assessment reflects exposure to parent iprodione. No quantitative postapplication cancer assessment has been completed for the iprodione degradate 3,5-DCA. The Q_1*for 3,5-DCA is not relevant to the residential postapplication exposure assessment (i.e., golfer scenario) since iprodione is metabolized to 3,5-DCA in drinking water.

Below are the algorithms and assumptions used to assess residential post-application exposure and cancer risk estimates. Exposure scenarios assessed include:

- Adult dermal exposure to treated golf course (adults/young adults)

Assumptions for Post-application Exposure Scenarios

General assumptions regarding the residential postapplication scenarios assessed are as follows:

- The body weight for cancer risk assessment is 80 kg
- HED has developed standard transfer coefficient (TC) values for residential post-application scenarios to ensure consistency in exposure assessments. These standard values were used to calculate post-application exposures. The TC for golfing exposure is 3400 cm^2/hr, when chemical-specific TTR data are used from a TTR study which used the modified California Roller technique.
- There are TTR data available for iprodione (MRID 44968001). The data were used as outlined above in Table 4.3.1.
- Duration of exposure on golf course lawns, greens and tees is assumed to be 4 hours. For the upper bound cancer assessment, it's assumed that golfers are exposed on greens for 1 hour and on fairways for 3 hours.
- It is assumed that 20 days per year are spent golfing based on golfing survey from United States Golf Association (USGA).
- Golfers are assumed to be in contact with golf course turf for approximately 50 years over a 78 year life time in determining cancer risk.

Similar to occupational handlers, cancer risk estimates were calculated using a linear low-dose extrapolation approach in which a Lifetime Average Daily Dose (LADD) is first calculated and then compared with a Q_1* that has been calculated for iprodione based on dose response data in the appropriate toxicology study (Q_1* = 0.0087 $(mg/kg/day)^{-1}$). Absorbed average daily dose (ADD) levels were used as the basis for calculating the LADD values. After the development of the ADD values, the next step required to calculate the carcinogenic risk is to amortize these values over the working lifetime of the occupational workers with postapplication exposure based on use pattern, which results in the LADD for that use. The Agency assumed postapplication exposure to treated golf courses could occur 20 days per year based on a golfing survey from USGA. Finally, 50 years of golfing activity in a 78 year lifespan were used to complete the calculations. LADD values were calculated using the following equation:

$$LADD = ADD \times \frac{\text{Exposure Frequency}}{\text{365 days/year}} \times \frac{\text{Activity Duration}}{\text{Lifetime}}$$

Where:

LADD (Lifetime Average Daily Dose) = the amount as absorbed dose received from exposure to a pesticide in a given scenario over a lifetime (mg pesticide active ingredient/kg body weight/day, also referred to as LADD),
ADD (Average Daily Dose) = the amount as absorbed dose received from exposure to a pesticide in a given scenario on a daily basis (mg pesticide active ingredient/kg body weight/day, also referred to as ADD),
Exposure Frequency = the annual frequency of exposure by an individual (days/year),
Activity Duration = the amount of a lifetime that an individual spends engaged in an activity (i.e. golfing) involving pesticide exposure (50 years), and
Lifetime = the average life expectancy of an individual (78 years).

Cancer Risk Estimates: Finally, cancer risk calculations were completed by comparing the LADD values calculated above to the Q_1* for iprodione (Q_1* = 0.044 $(mg/kg/day)^{-1}$). Cancer risk values were calculated using the following equation:

Cancer Risk Estimate = Dermal LADD (mg/kg/day) * Q_1* $(mg/kg/day)^{-1}$

Where:
Risk = Probability of excess cancer cases over a lifetime (unitless),
Dermal Lifetime Average Daily Dose = The amount as absorbed dose received from dermal exposure to a pesticide in a given scenario over a lifetime (mg pesticide active ingredient/kg body weight/day, also referred to as LADD), and
Q_1* = Quantitative dose response factor used for linear, low dose response cancer risk calculations $(mg/kg/day)^{-1}$.

Table 4.4B: Residential Postapplication Cancer Dermal Exposure and Risk with Q1* value of 0.044:

Scenario	TTR [A] (ug/cm2)	CF (mg/µg)	Tc (cm^2/hr)	ET (hrs)	BW (kg)	Dose [B] (mg/kg/day)	LADD [C] mg/kg/day	Cancer Risk [D]
Average Application Rate								
Adult Golfer 14-day TTR avging	0.22	0.001	5300	4	80	0.0029	0.000102	4.5×10^{-6}
Adult Golfer 28-day TTR avging	0.15	0.001	5300	4	80	0.0020	0.000072	3.2×10^{-6}
Upper Bound Application Rate								
Adult Golfer 14-day TTR avging	Greens - 1.984 Fairways - 0.49	0.001	5300	4	80	0.0049	0.000403	1.8×10^{-5}

A. Turf Transferable Residues (TTR) from study MRID 44968001.

B. Dermal Dose (mg/kg/day) = $\frac{\text{TTR } (\mu g/cm^2) \times 0.001 \text{ (mg/µg)} \times \text{TC } (cm^2/hr) \times \text{ET (hr/day)} \times 5\% \text{ DA}}{\text{BW (80 kg)}}$

C. Life Average Daily Dose (LADD) = Daily Dose (mg/kg/day) x $\frac{20 \text{ days}}{365 \text{ days}} \times \frac{50 \text{ years}}{78 \text{ lifetime years}}$

D. Cancer Risk = Q_1* (4.4×10^{-2} $mg/kg/day^{-1}$) x LADD (mg/kg/day)

The refined residential post-application cancer assessment assumes that a golfer is exposed to the same residue pattern 20 golfing days per year over 50 years of assumed golf play activity. The risk estimates range from 3.2×10^{-6} to 1.8×10^{-5}. This assessment involves significant refinement over a screening level assessment. Refinements include the use of TTR data, average application rates to reflect an individuals' lifetime exposure, and residue averaging based on likely product application parameters.

The product in the TTR study (Chipco® 26GT) is one of the most widely used products for turf, and is a good representative end use product for the TTR data. The 14- and 28-day average transferable turf residues were used to calculate the cancer risk estimates. The product label suggests application intervals of 14 to 28 days; cancer risk estimates are presented as a range based on: 1) an upper bound cancer risk estimate based on maximum label application rates and 2) 14-day and 28-day TTR averages of an average iprodione application rate.

Sometimes meteorological information like rainfall events, or turf treatment regimes can be used to characterize an exposure assessment using a TTR data set. The study report doesn't identify any out of the ordinary issues that would limit the use of this study for use in human health risk assessment. Both the timing of rainfall events and the timing of turf mowing are unclear from the iprodione TTR study report. The study report indicated some precipitation during the TTR study. The treated turf received care similar to standard industrial turf through typical irrigation and mowing procedures.

5.0 Label Recommendation

The product label includes several established uses and proposed new uses on curcurbits. The proposed label (86153-3) includes general product directions for both foliar and pre-plant/soil-incorporated directions for various crops. The label section for the proposed new curcurbit uses instructs users on the pre-plant and soil-incorporated applications. There are no instructions for foliar applications for curcurbits; therefore, this assessment did not include a quantitative occupational postapplication assessment for curcurbits. Based on the proposed use pattern, the proposed product label should be additionally modified to clarify that foliar application is prohibited for the proposed new uses on curcurbits.

APPENDIX A: IPRODIONE DFR STUDY SUMMARYAppendix A: Summaries of Dislodgeable Foliar Residue Studies and Proposed Use in Assessment

DFR Studies Available:

Iprodione: Review of *Iprodione: Determination of Transferable Turf Residues on Turf Treated with CHIPCO® 26GT*, TAF 0-5, MRID 44968001.
(HED Review: Review of "Determination of Transferable Turf Residue Dissipation from Turf Treated with Iprodione" , 04/27/2011, D389183)

The chemical-specific TTR study included three field trial sites in Georgia, California, and New York. The study was conducted on turf to evaluate the decline of iprodione equivalent residue (i.e., parent + metabolite) after six applications of a flowable concentrate iprodione product at a maximum application rate of 5.45 lbs ai/A/application. The re-treatment interval was approximately 14 days. The Modified California Roller technique was used to evaluate the amount of transferable residues from turf grass. A summary of the California site TTR values used in the residential exposure assessment is provided in Table A.

There are TTR data available for iprodione (MRID 44968001). Six applications of 5.45 lb iprodione/A in flowable concentrate formulation were applied by groundboom in three test sites, GA, CA, and NY. The highest TTR value from the Georgia site was 5 days after the sixth application; the TTR was 0.63 ug/cm^2. The 14 day average TTR value after 6 applications was 0.3506 ug/cm^2. The highest TTR value from the California site was 3 days after the sixth application; the TTR was 0.848 ug/cm^2. The 14 day average was 0.4924 ug/cm^2. The highest TTR value from the New York site was 8-12 hours after the sixth application; the TTR was 0.608 ug/cm^2. The 14 day average was 0.4457 ug/cm^2.

Peak residue formation occurred at 5DAT6 in Georgia, 3DAT6 in California, and 8-12 hrs DAT6 in New York. This phenomenon could possibly be explained by the delayed formation of the iprodione metabolite. The dissipation was only followed for 14 days, and the residues never reached levels less than the LOQ during the timeframe of the study. Immediately following the last application of the test product, the percentage of the original application rate of iprodione transferable to cotton sheeting material was 0.81% for the Georgia site, 1.12% for the California site, and 0.83% for the New York site.

First-order dissipation kinetics were assumed to generate dissipation curves for iprodione. The individual data points (rather than averages) from postapplication to 14DAT6 at the Georgia and California test sites. Due to the extreme variability in TTR for individual days at the New York test site, use of individual data points for regression analysis was not appropriate. Average daily data points were most appropriate for the New York site.

The estimated half-life values were 8.1 days (R^2=0.777) for Georgia, 9.8 days (R^2=0.618) for California, and 20.7 days (R^2 = 0.626) for the New York turf. While the Registrant did not correct for field recoveries, their calculated half-lives were similar to Agency calculated half-lives.

This study is acceptable to be used for risk assessment purposes.

Table A: Summary of Predicted TTR Levels Used in Residential Exposure Assessment (5.5 lbs ai/A unadjusted application rate)

Days after last Treatment	CA Site Mean Residue (ug/cm2)
0	0.777
1	0.724
2	0.674
3	0.628
4	0.585
5	0.545
6	0.508
7	0.474
8	0.441
9	0.411
10	0.383
11	0.357
12	0.333
13	0.310
14	0.289
15	0.269
16	0.251
17	0.234
18	0.218
19	0.203
20	0.189
21	0.176
22	0.164
23	0.153
24	0.143
25	0.133
26	0.124
27	0.115
28	0.107